Performance Monitoring Of Diabetic Patient Systems

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Abstract – **The minimum variance performance measure is applied to two diabetic patient models under simulated fault scenarios. The Bergman Model and the Automated Insulin Dosage Advisor (AIDA), are controlled in the Internal Model Control (IMC) framework to achieve adequate blood glucose levels. The focus of this paper is to reflect the importance and feasibility of implementing a detection and diagnosis tool such as the minimum variance performance benchmark to an implantable device for diabetics to guarantee adequate control of blood glucose levels.**
Keywords- **diabetes, Internal Model Control, minimum variance, performance assessment**

I. INTRODUCTION

With the advent of implantable insulin infusion pumps, normoglycaemia can be approached to help prevent diabetic complications [1]. However, like any mechanical device, malfunction is unavoidable and a measure of performance is necessary to detect any failure that could potentially violate the hypoglycaemic and hyperglycaemic bounds of the diabetic patient. In this paper, we consider two diabetic patient models, the Bergman model and the Automated Insulin Dosage Advisor ($AIDA$), which are controlled in the Internal Model Control (IMC) framework to maintain proper glucose levels. The performance of these models is assessed using the Harris minimum variance performance benchmark. Fault scenarios are proposed and simulated for the models to assess controller performance degradation.

With any model used for control design, it is essential to capture the most important dynamics of the system. This is the goal of both the Bergman and the AIDA models. Due to the simplicity of these models, a model-based control strategy can be implemented with a first order approximation of both models. The performance of these single-input single-output systems can be assessed in conjunction with a process delay that is due to the dynamics of the glucose sensor.

A. Bergman Model

The Bergman and AIDA models both utilize a "minimal model" approach to quantify the physiology of glucose and insulin. The Bergman Model is a two compartment model of glucose and insulin interactions [2]. The glucose pool accounts for glucose disappearance in the system (Equation (1)) while the insulin compartment describes insulin kinetics in the model, (Equation (2)). Insulin enters the system intravenously to mediate glucose uptake and production in the liver and periphery tissues. The model is described by the following equations:

$$\frac{dG(t)}{dt} = (P_1 - X)G(t) - P_1 G_b \tag{1}$$

$$\frac{dX(t)}{dt} = P_2 X(t) + P_3 I(t)$$

$$\frac{dI(t)}{dt} = \gamma(G(t) - h)t - nI(t) \tag{2}$$

where, X(t) represents insulin in the remote insulin compartment and I(t) models the second phase insulin kinetics in the model. The parameters of the model are P_1, P_2, P_3, n, h, and γ. The insulin sensitivity parameter, S_I, is given by $-P_3/P_2$ to represent the rate of glucose disappearance with respect to insulin concentration. The beta cell sensitivity of an individual is characterized by the first phase, $P_1/\Delta G$, and second phase, γ, sensitivity to glucose. The parameters n and h represent the time constant for insulin disappearance and the glucose threshold level, respectively. The fundamental nature of the model allows a quantitative assessment of the insulin and beta cell sensitivities of the diabetic patient.

B. Automated Insulin Dosage Advisor (AIDA)

The Automated Insulin Dosage Advisor ($AIDA$) is a three compartment model that was proposed by Lehmann and Deutsch to reflect the physiology of insulin action and carbohydrate absorption [3]. This model provides a 24-hour profile of glucose and insulin dynamics. The plasma insulin compartment represents the subcutaneous insulin absorption dynamics from an injection. The active insulin compartment contributes to the peripheral glucose uptake and the net hepatic glucose balance. The plasma glucose compartment is responsible for the overall glucose balance in the system. The simplicity of the model allows a patient to be characterized by two parameters which represent the hepatic, S_h, and peripheral, S_p, insulin sensitivities of an individual. Unique to this model is the characterization of the meal input by a trapezoidal time dependent function. The insulin dynamics of the model are given by:

$$\frac{dI}{dt} = \frac{Iabs}{V_i} - k_e t \tag{3}$$

$$\frac{dI_a}{dt} = (k_1 I) - (k_2 I_a)$$

$$I_{abs}(t) = \frac{stT_{50}^s D}{t[T_{50}^s + t^s]^2} \tag{4}$$

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Abstract

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$$T_{50} = aD + b$$

$$I_{a,ss}(t) = I_a(t) + I_a(t-24) + I_a(t-48) \quad (5)$$

$$I_{eq}(t) = k_2 \frac{I_{a,ss}(t)}{k_1} \quad (6)$$

where, k_1, k_2, and k_e represent insulin pharmacodynamic parameters and insulin elimination parameters, respectively. The subcutaneous insulin dynamics are given by the insulin absorption dynamics, $I_{abs}(t)$ and the half-life for insulin absorption, T_{50}. Parameters, a, b and s characterize how the dose of insulin injected, D, varies with the type of insulin administered to the patient [4]. I_{eq} represents the insulin level in equillibrium with $I_{a,ss}$. The glucose dynamics, G, are given below:

$$\frac{dG}{dt} = \frac{G_{in}(t) + NHGB(t) - G_{out}(t) - G_{ren}(t)}{V_g} \quad (7)$$

$$G_{out}(G, I_{eq}) = \frac{G(cS_pI_{eq} + GI)(K_m + GX)}{GX(K_m + G)} \quad (8)$$

$$\frac{G_{gut}}{dt} = G_{empt} - K_{gabs}G_{gut} \quad (9)$$

$$G_{in} = K_{gabs}G_{gut} \quad (10)$$

$$G_{ren} = GFR(G - RTG) \quad (11)$$

Equation (8) represents the overall rate of peripheral and insulin-independent glucose utilization where GI is the insulin-independent glucose utilization with reference value equal to GX, and K_m and c are the Michaelis Menten constant and peripheral glucose utilisation per insulin amount, respectively. The glucose amount in the gut after a meal intake is a function of the trapezoidal gastric emptying function, G_{empt}. The glucose input from the gut wall, G_{in}, is a function of G_{gut} with rate constant, K_{gabs}, for glucose absorption from the gut. The renal threshold of glucose, RTG, and the glomerular filtration rate, GFR, describe the rate of renal glucose excretion in the body. All of these affect the time course of glucose given by (7) which is also a function of the net hepatic glucose balance, $NHGB$.

In both models, neither glucagon dynamics nor the effects of exercise and other physiological states are considered in the system representation.

C. Internal Model Control

Internal Model Control (IMC) is the framework used to maintain adequate blood glucose levels, $70-100mg/dl$, in the diabetic system [5]. Therefore, a good approximation of the diabetic patient will determine the capability of the controller. In the IMC framework, the concept of perfect control is possible if the controller is designed as an exact inversion of the process with a known disturbance. In reality, this is never the case and the best approximation of the process must be made to achieve reasonable performance.

A first order approximation, $\tilde{g}(s)$, of both the Bergman and AIDA models is used for the control strategy. Since the model transfer function is invertible, the controller, $c(s)$, is given by:

$$c(s) = \frac{1}{\tilde{g}(s)} f(s) \quad (12)$$

$$f(s) = \frac{1}{(\lambda s + 1)^n} \quad (13)$$

where $f(s)$ is a filter with tuning parameters λ and n such that $c(s)$ is proper. The IMC strategy does not address input constraints, however, adequate blood glucose levels are acheived using this model-based control strategy.

D. Performance Monitoring

The foundation of controller performance monitoring tools are derived from the Harris minimum variance performance benchmark [6]. The idea behind this approach is that the process can be described by a linear transfer function with an additive disturbance, D_t, as in (14).

$$y_t = \frac{\omega(q^{-1})q^{-d}}{\delta(q^{-1})} U_t + D_t \quad (14)$$

where, ω and δ are polynomials in the backshift operator, q^{-1}. The linear feedback controller, U_t, is given by (12). With knowledge of the process delay, d, a time-series model is fit to the output data as in (15), where f is the time series coefficient and a_t is a white noise sequence [7].

$$\begin{aligned} y_t &= \underbrace{f_o a_t + f_1 a_{t-1} + \ldots + f_{d-1} a_{t-(d-1)}}_{e_t} \\ &\quad + f_d a_{t-d} + f_{d+1} a_{t-(d+1)} + \ldots \end{aligned} \quad (15)$$

Equation (15) can be separated into two parts. The first part, e_t, represents the minimum variance portion of the output data where values preceding the system delay are invariant of feedback control. The second part represents the portion of the output data after the delay which is dependent on the controller. Once the delay of the system is known, the performance index can be determined as the ratio of the minimum variance, σ^2_{mv}, to the actual variance, σ^2_y [8]:

$$\eta(d) = \frac{\sigma^2_{mv}}{\sigma^2_y} \quad (16)$$

A value of $\eta(d)$ close to zero indicates the potential to improve controller performance [9]. This can be approached by re-tuning the controller, changing the control strategy, or re-designing the process. Values of $\eta(d)$ near one indicate optimal controller performance in terms of minimum variance control. The main limitations of the minimum variance performance index are:

1. The performance index only addresses the process delay as the performance limiting factor.

2. Minimum variance may not be the control objective.
3. Extensions to the multivariate problem are difficult in characterizing the process delay.

More intricate measures would require more process information of the process which may not be feasible.

II. RESULTS AND DISCUSSION

Several variables can contribute to insulin pump failure. Any change in the overall system behavior (patient, pump, or sensor) will lead to performance degradation. Problems can arise as a result of a faulty glucose sensor that can yield biased and unreliable measurements. Depending on the insulin used and storage conditions, insulin aggregation could clog the pump and prevent proper insulin dosage. On the other hand, the controller could fail which would also yield improper insulin administration to the patient. Along those lines, patient variability may cause drifts/changes in model parameters that will contribute to controller failure.

Within the IMC framework, both the Bergman and AIDA models can be controlled within acceptable tolerances. The simulated faults are stochastic disturbances with zero mean noise and variance, σ^2. Glucose sensor failure is simulated by introducing the disturbance to the sensor measurement. To simulate controller failure, a disturbance is introduced to the system as the insulin input to the patient. Once the faults are introduced to the system, the data is filtered to remove the effects of the meal disturbance by computing the residual between the nominal plant and the perturbed plant. An Auto-regressive Moving Average ($ARMA$) time series model is fit to the output data and the performance index is determined.

A. Bergman Model

1. *Glucose Sensor Failure*–Figure 1 depicts a one week simulation of the diabetic patient with three 50g meals each day. The fault is introduced on day four to compare the nominal pump operation with the malfunctioning pump performance. With the introduction of the sensor failure, severe oscillations are observed in the glucose profile. As a result of improper glucose measurements, the mean performance index decreases 40 percent from the nominal.
2. *Controller Failure*– Figure 2 depicts a one week profile of the Bergman model with the controller failure beginning on day four. Most notable is the absence of any disturbance in the glucose profile. While this does not indicate a fault in the sytem, the plot of the performance index is able to detect improper insulin administration to the patient model due to excessive control action. This is observed by the severe oscillations in the index and notable performance degradation.

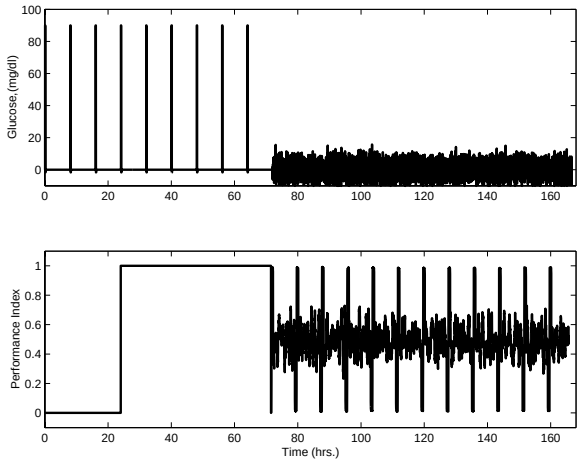

Fig. 1. Effect of glucose sensor failure on glucose profile (top) and preformance index (bottom).

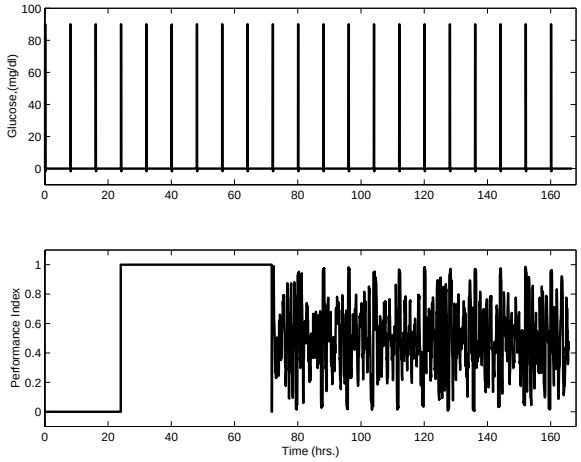

Fig. 2. Effect of controller failure on glucose profile (top) and performance index (bottom).

For the AIDA model, glucose sensor failure is simulated by the introduction of the disturbance to the sensor measurement, as in the Bergman model. To evaluate the sensitivity of the AIDA model to variations in parameters such as the hepatic insulin sensitivity, S_h, the parameter was varied from 0 to 1 throughout the course of a 24 hour day. Sensitivity values near 0 indicate a patient insensitive to insulin with little impact on glucose levels whereas an S_h value near 1 indicates a high correlation between insulin and glucose levels.

B. AIDA Model

1. *Glucose Sensor Failure*–Figure 3 shows a 24 hour profile of a diabetic patient with three 50g meals per day. At 1600 hrs, the glucose sensor fails producing the variations seen in the glucose profile. As a result, the performance index decreases with an oscillatory nature, indicative of preformance degradation in the

system.

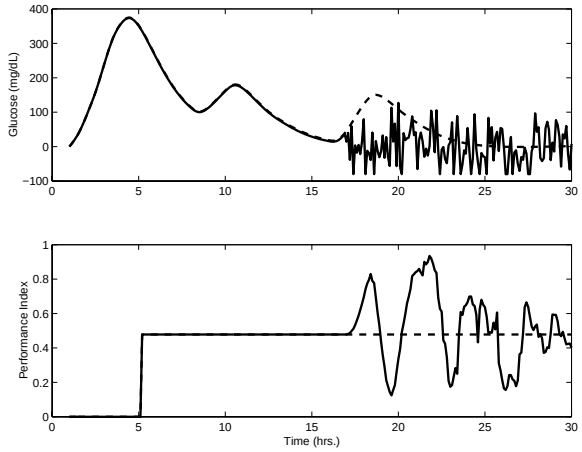

Fig. 3. Effect of glucose sensor failure on glucose profile (top) and performance index (bottom) ((dashed)-nominal model, (solid)-perturbed model).

2. *Variation in hepatic insulin sensitivity,* S_h–Figure 4 is a 24 hour profile of a diabetic patient that is almost completely insensitive to insulin in the hepatic tissue, $S_h = 0.1$. As a result, the glucose levels remain quite high. Over time, the patient becomes more sensitive to insulin resulting in lower blood glucose levels. Consequently, the glucose profile indicates better regulation of levels and this manifests itself in the performance index calculation.

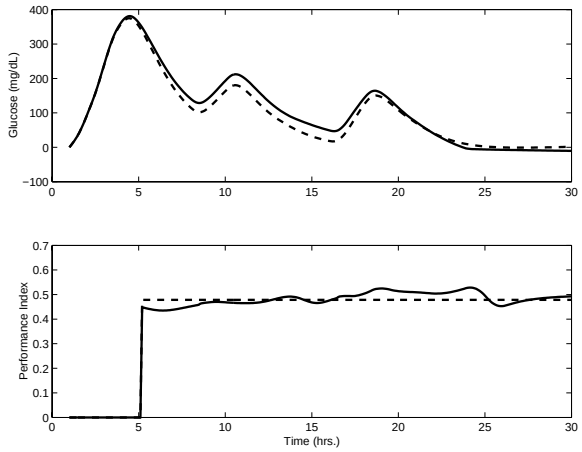

Fig. 4. Effect of parameter variation, S_h, on glucose profile (top) and performance index (bottom) ((dashed)-nominal model, (solid)-perturbed model).

Oscillations and abrupt changes in the mean performance index may indicate faults requiring immediate attention e.g., sensor and controller failure. In contrast, gradual deviations from the mean performance index showing a trend may indicate less series faults that over time could get worse e.g., parameter drifts.

III. CONCLUSIONS

Both the Bergman and AIDA models provide benchmark simulations of the diabetic patient system. Further work in quantifying higher order dynamics such as the effects of glucagon, exercise or stress in the system is necessary not only from a modeling perspective but, also in the development of an effective control algorithm. Using IMC for both patient systems provides the basis for a more advanced control strategy, such as Model Predictive Control (MPC). The key in controlling diabetes is the minimization of the hypoglycaemic and hyperglycemic excursions in the glucose profile of the patient. Model Predictive Control has had success in handling input and output constraints in diabetes applications [10]. The diabetic process warrants the use of an MPC algorithm to prevent complications such as coma, death and retinopathy as a direct result of violating these bounds. In regulating the system, at all times, the safety of the patient must be guaranteed by monitoring the performance of the controller. At present, the Harris minimum variance benchmark provides a tool that has been widely implemented and practiced to assess controller performance.

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